

## Cardiovascular journals



### All-cause mortality in type 2 diabetes: It's all about the eGFR and not the serum creatinine

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The prevalence of chronic kidney disease is around four times greater in people with diagnosed diabetes than people without (39.6% vs 10.6%; Plantiga et al, 2010).

I have been slow to catch on to the importance of the estimated glomerular filtration rate (eGFR) as a marker of renal dysfunction in people with diabetes, having previously been perfectly happy using serum creatinine levels. I have paid a lot more attention to the transition from normoalbuminuria to microalbuminuria, and then to proteinuria as higher stages herald increased risk of cardiovascular disease and need for end-stage renal replacement, such as haemodialysis or renal transplantation.

In the study summarised alongside, Fabbian et al report on the all-cause mortality and estimated renal function over an average 9.8 years. A large cohort of 1365 consecutive out-patients with type 2 diabetes were investigated in a prospective, longitudinal, observational study to explore the relationship between serum creatinine and several eGFR equations. All-cause mortality was the primary end-point used, and the mean age of the study cohort was 58 years. The only exclusion criterion was the use of renal replacement therapy.

Several of the eGFR equations used for the analyses included: Modification of Diet in Renal Disease (MDRD)186 formula, MDRD175 formula, Mayo Clinic Quadratic formula and the Cockcroft–Gault formula. As seen in previous studies, a diagnosis of nephropathy was associated with a significantly increased risk of all-cause mortality (odd ratio 2.55; Zoppini et al, 2012).

Nephropathy and microvascular complications were more prevalent in people who died versus survivors (41.4% vs 20.6% respectively). Receiving operating characteristic (ROC) analyses showed that all-cause mortality was better, and more significantly, predicted by a low eGFR (using any equation) than the serum creatinine value alone.

What does this mean for clinical practice? It means we have to throw out the serum creatinine as this is a crude “univariate” indicator of renal function that does not take into consideration age, sex, and ethnicity (if African-Caribbean).

In the biblical story of Job, Job complains that “physicians [are] of no value” (Job 13:4) when his “reins were consumed within me” (Job 19:27) (Eknayan, 2005). In 2015, we have plenty of opportunities to reduce the morbidity and mortality associated with diabetic kidney disease by focusing on improving glycaemic control and control of blood pressure to a systolic  $\leq 130$  mmHg, and by appropriate evidence-based use of drugs such as losartan, irbesartan, ramipril and statins. However, using the eGFR as a measure of renal function rather the serum creatinine is more important. ■

Eknayan G (2005) The kidneys in the Bible: what happened? *J Am Soc Nephrol* **16**: 3464–71

Plantiga LC, Crews DC, Coresh J et al (2010) Prevalence of CKD in US adults with undiagnosed diabetes or prediabetes. *Clin J Am Soc Nephrol* **5**: 673–82

Zoppini G, Targher G, Chonchol M et al (2012) Serum uric acid levels and incident chronic kidney disease in patients with type 2 diabetes and preserved kidney function. *Diabetes Care* **35**: 99–104

### Diab Vasc Dis Res

### eGFR: A better predictor of all-cause mortality than serum creatinine?

Readability ////

Applicability to practice ////

WOW! Factor ////

**1** The relationship between renal function and all-cause mortality (ACM) was investigated with both estimated glomerular filtration rate (eGFR) and serum creatinine (SCr).

**2** The cohort were a group of 1365 consecutive out-patients with T2D who were followed for  $9.8 \pm 3$  years. Their mean age was  $58 \pm 10$  years. In total, 296 people had a diagnosis of nephropathy, 153 had microalbuminuria and 36 had macroalbuminuria. Seventy (5.1%) people died during follow-up, and the majority of deaths were due to cardiovascular events (85%).

**3** Six different equations for eGFR were used to evaluate renal function of the participants (MDRD186 formula, MDRD175 formula, Mayo Clinic Quadratic formula, CKD-EPI formula, Cockcroft–Gault formula and Schaeffner’s equation). Blood samples were taken to measure SCr, as well as other biochemical markers.

**4** Nephropathy and microvascular complications were associated with ACM.

**5** Receiving operating characteristic (ROC) curves showed that the areas under the curve for ACM were similar using the different eGFR equations, but not for SCr.

**6** The authors did not aim to precisely calculate renal function in order to classify kidney damage, rather to evaluate the prognostic impact of different equations on ACM in people with T2D.

Fabbian F, De Giorgi A, Monesi M et al (2015) All-cause mortality and estimated renal function in type 2 diabetes mellitus outpatients: Is there a relationship with the equation used? *Diab Vasc Dis Res* **12**: 46–52

## Am Heart J

### Indapamide versus hydrochlorothiazide: Arterial function

Readability ///

Applicability to practice ////

WOW! Factor ///

**1** Indapamide and hydrochlorothiazide are both diuretics and are added to an angiotensin-converting enzyme inhibitor for the treatment of hypertension.

**2** Their effect on ventricular and arterial functions in people with T2D and hypertension were investigated.

**3** A prospective, randomised, active-controlled, blinded one end study in 56 people with mild-to-moderate hypertension and T2D was carried out. Participants were randomised to either indapamide (1.5 mg Slow Release/day) or hydrochlorothiazide (25 mg/dL), added to quinapril (10–40 mg/dL).

**4** The baseline characteristics were similar between groups. After 6 months, systolic and diastolic blood pressures decreased similarly for indapamide and hydrochlorothiazide. Mean longitudinal systolic velocity, mean longitudinal early diastolic velocity and longitudinal strain all increased on indapamide, but did not change on hydrochlorothiazide ( $P < 0.05$  for intergroup differences).

**5** Indapamide improved measures of endothelial and arterial functions in people with diabetes and hypertension, and may have important vascular effects that can improve ventriculoarterial coupling.

**6** The authors conclude that the results of this study add to the general debate over whether different pharmacological treatments offering similar blood pressure control might have differences that could impact clinical outcomes.

Vinereanu D, Dulgheru R, Magda S et al (2014) The effect of indapamide versus hydrochlorothiazide on ventricular and arterial function in patients with hypertension and diabetes. *Am Heart J* **168**: 446–56

## Int J Cardiol

### HMG-CoA reductase inhibitors: Cerebrovascular attack prevention

Readability ///

Applicability to practice ////

WOW! Factor ////

**1** HMG-CoA inhibitors are known to reduce ischaemic heart disease (IHD) in middle-aged people with T2D, but their preventative effects on cerebrovascular attack (CVA) among late elderly ( $\geq 75$  years) people has not been investigated so thoroughly, due to the difficulty in conducting randomised controlled trials in an older population.

**2** A prospective case-cohort study was conducted in Japan with 5.5 years of follow-up from 2009. In total, 4014 people with T2D without previous IHD or CVA were included along with a sub-cohort of 405 people who had a history of IHD or CVA.

**3** Medical records and laboratory data of participants were analysed after every medicine change, and statin-users were sub-divided into prevalent (over 5.5 years use), new (less than 5.5 years use) and non-users.

**4** A total of 104 CVAs occurred during the follow-up period among people who had previously had a CVA or IHD event. In the case-control analysis, there was increased prevalence of CVAs among those that were non-statin users in an age-dependent manner.

**5** Interestingly, CVA incidence was lower in prevalent and new statin-users (hazard ratio [HR] 0.46, 0.523), especially in late elderly (HR; 0.51, 0.21).

**6** The authors conclude that statins have a direct effect on HDL-cholesterol and glucose metabolism, which may reduce the incidence of CVA in late elderly people with diabetes.

Hayashi T, Kubota K, Kawashima S et al (2014) Efficacy of HMG-CoA reductase inhibitors in the prevention of cerebrovascular attack in 1016 patients older than 75 years among 4014 type 2 diabetic individuals. *Int J Cardiol* **177**: 860–6

## Int J Cardiol

### U-shaped association: Blood pressure and heart failure among people with diabetes

Readability ///

Applicability to practice ////

WOW! Factor ///

**1** Guidelines from Europe and the US recommend that blood pressure (BP) targets should be more aggressive for people with T2D ( $< 140/80$  mmHg or  $140/85$  mmHg) than for people without the condition ( $< 140/90$  mmHg).

**2** BP control has been shown to reduce the risk of heart failure (HF), although it is not known whether the lowest clinical BP achieved ultimately results in the lowest risk of HF in people with diabetes.

**3** A large prospective cohort study of 17 181 African Americans and 12 446 white people with diabetes who did not have coronary heart disease or HF at diabetes diagnosis were included in the study.

**4** During a mean follow-up of 6.5 years, 5089 incidences of HF cases were identified.

**5** A U-shaped association was confirmed between observed BP and the risk of HF in the cohort.

**6** Both a low BP at baseline ( $< 120/70$  mmHg) and follow-up ( $< 130/80$  mmHg) and uncontrolled high BP at baseline ( $\geq 160/100$  mmHg) and follow-up ( $\geq 140/90$  mmHg) are associated with an increased risk of HF for African Americans and white people.

**7** A secondary finding was that there is a linear association between increasing pulse pressure and incidence HF risk in the cohort.

**8** Furthermore, the U-shaped association was more significant in people with diabetes aged 30–49 years and 50–59 years.

Zhao W, Katzmarzyk PT, Horswell R et al (2014) Blood pressure and heart failure risk among diabetic patients. *Int J Cardiol* **176**: 125–32

“Both a low blood pressure an uncontrolled high blood-pressure at baseline and follow-up years later are associated with an increased risk of heart failure for people with diabetes.”